PATENT
2809-0123P

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant: ICHIKAWA et al. Conf.:

Appl. No.: NEW Group: Unassigned

Filed: November 8, 2001 Examiner: Unassigned

For: METHOD OF PREPARING LOW ALLERGIC NATURAL RUBBER LATEX AND DEPROTEINIZED NATURAL RUBBER LATEX, AND LOW ALLERGIC NATURAL RUBBER AND DEPROTEINIZED NATURAL RUBBER

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, DC 20231

November 8, 2001

Sir:

The following preliminary amendments and remarks are respectfully submitted in connection with the above-identified application.

IN THE SPECIFICATION:

Please replace the paragraph beginning on page 2, line 25, with the following rewritten paragraph:

--In case of subjecting to the deproteinization treatment by the method described in the above publication, an infrared

absorption spectrum at 3280cm^{-1} peculiar to polypeptide is not observed in a rubber film formed by using the treated natural rubber latex. Therefore, it has been found that decomposition and removal of the protein are highly achieved by the method described in the above publication.--

Please replace the paragraph beginning on page 8, line 8, with the following rewritten paragraph:

--From another point of view, the present inventors have made a trial of performing a decomposition treatment of a protein using a protease having an exopeptidase activity and a removing treatment of the protein and the protein decomposition product thereof, in addition to the decomposition treatment of the protein using a conventional alkali protease. As a result, they have surprisingly found a novel fact that the protein can be decomposed and removed to such a degree that the protein and the protein decomposition product, which have a number-average molecular weight <Mn> of 4500 or more do not substantially exist, thereby making it possible to obtain a deproteinized rubber latex which is less likely to cause allergy. Thus, the invention (II) of the above-described method of preparing a low allergic natural rubber latex has been completed.--

Please replace the paragraph beginning on page 10, line 2, with the following rewritten paragraph:

--In the method of preparing a deproteinized natural rubber latex of the present invention (II), it is preferred to remove the protein and the decomposition product thereof by a centrifugation treatment in view of the removing effect and the efficiency of the removing treatment.--

Please replace the paragraph beginning on page 31, line 11, with the following rewritten paragraph:

--(16) The method of preparing a deproteinized natural rubber latex described in the term (13), wherein the microorganisms which belong to the genus Rhizopus are microorganisms which belong to *Rhizopus oryzae*.--

Please replace the paragraph beginning on page 37, line 17, with the following rewritten paragraph:

--C. The method (III) of preparing a low allergic natural rubber latex of the present invention will be described.--

Please replace the paragraph beginning on page 39, line 4, with the following rewritten paragraph:

--The low allergic natural rubber of the present invention has a feature that it is obtained by performing a decomposition treatment of a protein by a protease having an exopeptidase activity. Surprisingly, the protein can be decomposed to such a degree that the protein and the protein decomposition product, which have a number-average molecular weight <Mn> of 4500 or more, do not substantially exist by performing a treatment using the protease.--

Please replace the paragraph beginning on page 75, line 2, with the following rewritten paragraph:

--With respect to the analysis results of the number-average molecular weight <Mn> about the remained protein and protein decomposition product, the measurement results of samples obtained from the deproteinized natural rubber latex of Example 7 are shown in Fig. 5, the measurement results of samples obtained from the deproteinized natural rubber latex of Example 8 are shown in Fig. 7, the measurement results of samples obtained from the deproteinized natural rubber latex of Example 9 are shown in Fig. 6, the measurement results of samples obtained from the deproteinized

natural rubber latex of Example 10 are shown in Fig. 8, and the measurement results of samples obtained from the deproteinized natural rubber latex of Comparative Example 2 by a conventional treatment using an enzyme are shown in Fig. 3, respectively.--

Please replace the paragraph beginning on page 75, line 16, with the following rewritten paragraph:

--The molecular weight of control samples obtained from the HA latex, which has been subjected to neither protein decomposition treatment nor protein removing treatment, was analyzed. The measurement results are shown in Fig. 4.--

Please replace the paragraph beginning on page 75, line 20, with the following rewritten paragraph:

--As is apparent from the measurement results of the analysis of the molecular weight, in Comparative Example 2 (Fig. 3), a peak existed at the position (position corresponding to the existence of the protein) where the number-average molecular weight <Mn> is about 4700. To the contrary, in Example 7 (Fig. 5) and Example 9 (Fig. 6), a peak was not observed in the range where the number-average molecular weight <Mn> is about 2000 or more. In Example 8 (Fig. 7)

and Example 10 (Fig. 8), a peak was not observed in the range where the number-average molecular weight <Mn> is 4500 or more.--

In the Claims:

Please replace the claim 16 with the following rewritten claim:

16. The method of preparing a deproteinized natural rubber latex according to claim 13, wherein the microorganisms which belong to the genus Rhizopus are microorganisms which belong to *Rhizopus oryzae*.

REMARKS

Claims 1-25 are pending in the present application.

Entry of the above amendments is earnestly solicited. An early and favorable first action on the merits is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the application by this Amendment.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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ADM/csp
2809-0123P

Attachments

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph beginning on page 2, line 25, has been amended as follows:

In case of subjecting to the deproteinization treatment by the method described in the above publication, an infrared absorption spectrum at ~~3280^{-1} cm~~ $3280cm^{-1}$ peculiar to polypeptide is not observed in a rubber film formed by using the treated natural rubber latex. Therefore, it has been found that decomposition and removal of the protein are highly achieved by the method described in the above publication.

The paragraph beginning on page 8, line 8, has been amended as follows:

From another point of view, the present inventors have made a trial of performing a decomposition treatment of a ~~protease~~ protein using a protease having an exopeptidase activity and a removing treatment of the protein and the protein decomposition product thereof, in addition to the decomposition treatment of the protein using a conventional alkali protease. As a result, they have surprisingly found a novel fact that the protein can be

decomposed and removed to such a degree that the protein and the protein decomposition product, which have a number-average molecular weight <Mn> of 4500 or more do not substantially exist, thereby making it possible to obtain a deproteinized rubber latex which is less likely to cause allergy. Thus, the invention (II) of the above-described method of preparing a low allergic natural rubber latex has been completed.

The paragraph beginning on page 10, line 2, has been amended as follows:

In the method of preparing a deproteinized natural rubber latex of the present invention (II), it is preferred to ~~decompose~~ remove the protein and the decomposition product thereof by a centrifugation treatment in view of the removing effect and the efficiency of the removing treatment.

The paragraph beginning on page 31, line 11, has been amended as follows:

(16) The method of preparing a ~~low allergic~~ deproteinized natural rubber latex described in the term (13), wherein the microorganisms which belong to the genus Rhizopus are microorganisms

which belong to *Rhizopus oryzae*.

The paragraph beginning on page 37, line 17, has been amended as follows:

C. The method (III) of preparing a ~~deproteinized~~ low allergic natural rubber latex of the present invention will be described.

The paragraph beginning on page 39, line 4, has been amended as follows:

The low allergic natural ~~natural~~ rubber of the present invention has a feature that it is obtained by performing a decomposition treatment of a protein by a protease having an exopeptidase activity. Surprisingly, the protein can be decomposed to such a degree that the protein and the protein decomposition product, which have a number-average molecular weight <Mn> of 4500 or more, do not substantially exist by performing a treatment using the protease.

The paragraph beginning on page 75, line 2, has been amended as follows:

With respect to the analysis results of the number-average molecular weight <Mn> about the remained protein and protein decomposition product, the measurement results of samples obtained from the deproteinized natural rubber latex of Example 7 are shown in Fig. 5, the measurement results of samples obtained from the deproteinized natural rubber latex of Example 8 are shown in Fig. 7, the measurement results of samples obtained from the deproteinized natural rubber latex of Example 9 are shown in Fig. 6, the measurement results of samples obtained from the deproteinized natural rubber latex of Example 10 are shown in Fig. 8, and the measurement results of samples obtained from the deproteinized natural rubber latex of Comparative Example 2 by a conventional treatment using an enzyme are shown in ~~Fig. 9~~ Fig. 3, respectively.

The paragraph beginning on page 75, line 16, has been amended as follows:

The molecular weight of control samples obtained from the HA latex, which has been subjected to neither protein decomposition treatment nor protein removing treatment, was analyzed. The measurement results are shown in ~~Fig. 10~~ Fig. 4.

The paragraph beginning on page 75, line 20, has been amended

as follows:

As is apparent from the measurement results of the analysis of the molecular weight, in Comparative Example 2 (~~Fig. 9~~ Fig. 3), a peak existed at the position (position corresponding to the existence of the protein) where the number-average molecular weight <Mn> is about 4700. To the contrary, in Example 7 (Fig. 5) and Example 9 (Fig. 6), a peak was not observed in the range where the number-average molecular weight <Mn> is about 2000 or more. In Example 8 (Fig. 7) and Example 10 (~~Fig. 4~~ Fig. 8), a peak was not observed in the range where the number-average molecular weight <Mn> is 4500 or more.

In the Claims:

Please amend the claims as follows:

16. The method of preparing a ~~low allergic~~ deproteinized natural rubber latex according to claim 13, wherein the microorganisms which belong to the genus Rhizopus are microorganisms which belong to *Rhizopus oryzae*.